eight to twelve weeks after infection, shortly after the appearance of general symptoms, and that it usually continues for four to eight weeks. Parrot again asserts that an enlarged spleen is nearly constant in, and one of the best signs of the malady in infants attacked with, inherited syphilis not having passed one month, but that after three months and especially six months this hypertrophy becomes exceptional. This point is obviously one of much importance in our inquiry, and our observations, as well as those of Barlow and others, are directly at variance with Parrot's conclusions with respect to the frequency of an enlarged spleen in inherited syphilis after three months. Haslund's observations also seem opposed to Parrot's in this matter. Both clinical and pathological evidence would appear to demonstrate that this splenic enlargement is often a chronic process.

We next present a table (as simple as possible to economise space) showing the ages at which the spleen was found enlarged in our cases of inherited syphilis. It is necessary to bear in mind the age at which the symptoms of syphilis usually evolve, and to note that many of the older infants had apparently never been treated previously. To all grey powder was administered, to some for considerable periods, to others only intermittently according to circumstances of their attendance, etc.

Ages at which the Spleen was observed to be Enlarged in Cases of Inherited Syphilis.—1 at 5, 6, and 6½ weeks respectively; 1 at 7 weeks (early R at 11 months; 7 at 2 months (in 1 almost, and 1 quite, to umbilicus, 1 R at 15 months); 1 at 8½ weeks (R at 14 months); 4 at 9 weeks (1 R at 8 months); 2 at 10 weeks (1 R at 9 months); 1 at 11 weeks (spleen to iliac crest); 10 at 3 months (in 3 R developed); 3 at 3½ months (in 1 R developed); 10 at 4 months (in 1 spleen to umbilicus, in 4 R developed); 7 at 5 months (in 2 spleen very large, in 2 R developed); 5 at 6 months (in 1 R); 4 at 7 months; 3 at 8 months, all rickety; 3 at 10 months, all rickety; 2 at 11 months (both rickety); 3 at 15 months, all rickety; 3 at 16 months, all rickety; 1 at 19 months, rickety; 2 at 2 years, both rickety. (The letter R stands for bone rickets, excluding craniotabes).

Of these 75 cases of syphilitic infants with enlarged spleen, all, with three exceptions only, of those who were kept under observation during the period when rickety bone changes become evident, developed rickets; and of those not having an appreciably enlarged spleen who were similarly observed, only about the same proportion failed to develop distinct rickety bone changes. We are thus led to confirm the opinions of Kassowitz and Fournier that rickets is observed with an incontestable degree of frequency in subjects attacked with inherited syphilis. In only one of our cases did the spleen begin to enlarge after the rickety bone changes became obvious, although in several the spleen increased notably in size as the rickets developed. Antisyphilitic treatment, with cod-liver oil and iron administered from the time the infants first came under observation, was undoubtedly followed by an early diminution in the size of the spleen in many cases, but in some this organ long remained stationary or slowly increased in bulk in spite of similar treatment.

To sum up: In 63 cases of splenic enlargement in infants we could not positively exclude the presence of rickets in a single one, and in almost all the rickets was clear and distinct. In 41 per cent. of the 63 cases inherited syphilis was undoubted, and in the remainder syphilis could neither be positively affirmed nor excluded. Of 155 cases of inherited syphilis the spleen was found by palpation to be enlarged at some period in 48.4 per cent., and it is universally accepted that enlargement of the spleen is of excessive frequency in inherited syphilis—at any rate in the earliest stages—and we assert that it may persist to later stages also. This enlargement is apparently often indistinguishable histologically from that met with in cases of rickets. Our observations confirm the opinion of Kassowitz and Fournier that rickets occurs with an incontestable degree of frequency in subjects attacked with inherited syphilis. In rickets the spleen is found enlarged in perhaps 25 per cent. of the cases. From these facts—and we present our observations with some confidence, as having been checked by two observers—we do not wish to draw any dogmatic conclusions. Bone changes constitute only one of the symptoms of rickets, and are not the earliest, so that, allowing for the frequency of enlarged spleens in early syphilis, the bulk of our cases may quite possibly be due to rickets, either primarily or engrafted upon syphilis. We think, however, that we are justified in saying that in every case of enlarged spleen in an infant, such as we have been discussing, there is reasonable ground for suspecting syphilis. We are not aware of any observations on the viscera and lymphatic glands in cases of rickets in animals, but such an inquiry seems to be very desirable as an aid to the solution of the vexed question under discussion.

Note.—Since this paper was written Mr. Bland Sutton has been kind enough to inform us that the spleen and liver are often, though not constantly, enlarged in rickety monkeys, especially in the very young ones.

ON SOME SYMPTOMS ASSOCIATED WITH THE URIC ACID DIATHESIS IN CHILDREN.

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The presence of uric acid, or oxalates, in the urine of children is such a familiar sight that by many it is regarded as the normal condition, or, at most, as the evidence of a slight stomachic derangement. The conditions of occurrence of uric acid and oxalates are so closely allied that, for clinical purposes, they may be taken together. These substances may be present in the system and in the urine for a considerable time without producing any symptoms to attract the notice of the patient's friends, and it is only on the occurrence of hæmaturia or severe abdominal pain that the physician is called in.

From a clinical standpoint, the symptoms may be classified as follows:—

1. *Symptoms Due to the Presence of Uric Acid in the System.*—The subjects of the diathesis are often easily recognised. They have keen precocious minds, and small restless bodies; they are excitable, nervous, bright and amusing at one time, and greatly depressed at another; they do not readily fall asleep at night, often talk in their sleep, and have a habit of awaking in the very early morning; and they are dainty feeders, with a taste for everything that is bad from a nutritious point of view. The children are often described by their parents as being very subject to colds, and a chill in some form or another is the usual precursor of an acute attack. Along with this, and acting possibly as the cause, is a tendency to profuse sweating on moderate heat or exertion. Cold hands and feet are very frequently complained of—a symptom which Dr. Haig ascribes to uric acid in the blood, and which, he suggests, may be found in a more advanced condition as the local asphyxia of Raynaud's disease. During the course of the affection acute attacks occur, which are recurrent in type and usually of short duration, especially if the child is kept in bed. The pharynx is often relaxed and irritable, causing a loud barking cough, most marked when the child goes to bed, and which may be accompanied by some bronchial inflammation. The tonsils and adenoid tissue of the naso-pharynx are liable to acute attacks, which lead to chronic thickening and enlargement. Frontal headache and symptoms of intestinal catarrh, with a furred tongue and foul breath are common. As regards the heart, a slight irregularity is occasionally found, and the pulse is often small, weak, and irregular. The liver and spleen may be enlarged. In some cases abdominal pain is the only complaint, and this may sometimes be found to be localised in the right iliac fossa.

2. *Symptoms due to the Excretion of Uric Acid from the System.*—Pain is one of the most prominent symptoms. Dr. Goodhart,[1] in the course of some remarks on the uric acid diathesis of childhood, says "renal colic is far commoner in children than is usually supposed, but it passes for stomach-ache pure and simple, and goes unrecognised." The pain may be present in any part of the urinary tract, from the kidney downwards. If the irritation is in one or both kidneys, pain is referred to the region affected, and is described as passing downwards and forwards in the line of the ureter, or it may be localised entirely at the umbilicus. The pain is intermittent in character, and is often so intense that the child will scream loudly, especially in the middle of the night. Hæmaturia (renal) is frequently the first symptom to cause alarm, and there may be more or less shivering, nausea, and sickness present during an attack. When the bladder is irritated and inflamed by the crystals and the ex-

[1] British Medical Journal, 1891, ii, p.251.

cessive acidity of the urine, the pain is suprapubic, and extends along the urethra to the meatus. It is often brought on by walking, and is increased during micturition, so that the urine is retained for a considerable time. I have never been able to trace a convulsive seizure to local irritation in the urinary tracts; but Henoch describes a case of convulsions in a child five months old, due to reflex irritation from extreme dysuria, accompanied by the passage of large uric acid crystals. As the kidneys are believed to secrete the uric acid from the blood, it is probable that great irritation may be caused in the tubules by the mechanical contact with the sharp particles. These may soon combine with the bases in the urine, are thus rendered non-irritant, and may be excreted without producing any disturbance in the urinary tract. Should the urine, however, contain only a small amount of these bases, or should the passage of the uric acid through the tubules be hastened, pain will probably be present; and this is what we find, for example, in the screaming at night, when the urine is most acid, and in the pain caused by walking, when, both from the vascular and muscular pressure, the kidneys are emptied of their contents more rapidly. The greater the proportion of solid to fluid constituents in the urine, the more marked will the pain be; while, if the watery constituents are abundant, pain will probably be entirely absent. It is a marked feature in the subjects of this diathesis that they drink in moderation, while they sweat profusely on slight exertion, with the result that the amount of urine passed is small.

Many cases of intractable incontinence are due to inflammation in the bladder, which is induced and kept up by the excessive acidity of the urine. Rectal pain, incontinence of fæces, pain during defæcation, prolapse of the rectum, and irregularity of the bowels will often be cured by directing treatment solely to the condition of the bladder and urine. This may be confirmed on rectal examination by the tenderness which is found on pressing forwards over the lower part of the bladder. Albuminuria is not infrequent, with or without hæmaturia, and is produced, like the latter, by mechanical irritation in the kidneys. The amount of albumen may vary from the merest trace up to one-half (on boiling), and tube casts may be present, usually fewer in number, and of a more limited variety than in albuminuria from organic structural disease of the kidneys. A catarrhal inflammation in the pelvis of the kidney, or about the neck of the bladder, is manifested by the appearance of pus cells in the urine, with epithelial scales. Dr. Milner Fothergill says that "a large deposit of urates is a storm signal," and these storm signals are of very great use in this latent disease. Case IX is an example of this. It is that of a girl, aged 10 years, who was apparently in good health, but whose urine contained urates and uric acid in such abundance as to attract special attention. This was soon followed by an attack of tonsillitis, pericarditis with delirium, endocarditis, and very severe chorea.

Most of the above symptoms are illustrated in the accompanying cases. There are some others in which the connection with uric acid may not be so readily admitted.

1. *Inflammation of the Vermiform Appendix* (Cases VI and VII).—Slight attacks of this trouble are very common in childhood, with, in many cases, a marked tendency to recur, and followed in a certain number by perforation, and local or general peritonitis. Mr. Bland Sutton has pointed out the anatomical similarity between the tonsils and the vermiform appendix, both being largely composed of adenoid tissue, and the pathological resemblance of simple and suppurative tonsillitis on the one hand, and simple and suppurative appendicitis on the other. On examining the urine carefully in cases of appendicitis I have found both uric acid and oxalates present in excess, along with other symptoms of the diathesis. Whether the calculi found in the appendix are of uric acid or oxalic acid I have not been able to learn, and possibly they are of the type often seen in the crypts of the tonsillar follicles. Quite recently Mr. Jordan Lloyd has recorded a case in which he removed a gangrenous vermiform appendix where, before operation, he suspected a calculus in the right ureter from the fact that the patient had suffered for some years from calculous nephralgia of the left kidney.

2. *Paroxysmal Hæmoglobinuria* presents amongst other characteristics those of periodicity in the attacks, and exposure to cold as the immediate cause. Case X is that of a boy, aged 5 years, who was admitted to Paddington Green Children's Hospital with a history of three months' illness, and complaining of headache, occasional sickness, loss of appetite, and hæmaturia. He had passed blood in his urine twice or thrice a week, and his mother noticed that this usually followed on some exposure to cold. He was the subject of hereditary syphilis and rickets. The child was markedly rachitic and very anæmic. The spleen was just palpable below the ribs, and the liver extended half way to the umbilicus. There was a hæmic murmur at the cardiac apex. He had several typical attacks of hæmoglobinuria while in the hospital, and occasionally albumen was present in the urine without any blood. During three weeks oxalates were constantly present in the urine in large amount. In a case of Raynaud's disease associated with paroxysmal hæmoglobinuria and excess of uric acid, Dr. Haig regarded the uric acid as the cause of the hæmoglobinuria by destruction of the red blood cells. In the same way the excess of oxalates in the blood may be a factor in producing the destruction of blood cells. The oxalates were constantly present in the urine, and not, as is frequently stated, only during an attack of hæmoglobinuria. Fagge refers to the intermittent albuminuria in many cases of paroxysmal hæmoglobinuria, and to the supervention of Bright's disease in one patient, both of which conditions might be produced by the irritation of uric acid or oxalates.

3. *Functional Albuminuria.*—Case VIII would come under this term, in the subdivision "cyclic." The patient was a girl, aged 7½ years, who, in addition to being "born with asthma," had suffered from measles, erysipelas, scarlet fever (two years previously), whooping-cough, chicken-pox, adenoid growths in the naso-pharynx, and vulvar irritation. During forty-two successive days every specimen of urine passed was examined by Mr. H. L. Lack, the house-surgeon at Paddington Green Children's Hospital. The urine was invariably acid, and albumen was present, varying in quantity from the merest trace up to one-half, on 133 out of 197 examinations. During 34 successive days, uric acid and urates were present on 20, and oxalates on 23 days, on naked eye or microscopic examination. The urine was usually of high specific gravity; the amount at first was very small, 10 or 12 ounces a day; and a large amount of uric acid or oxalates was accompanied by a corresponding increase in the amount of albumen. No casts or pus cells were ever detected in the urine. The albuminuria was increased by walking exercise, and the internal administration of iron, while it was diminished by absolute rest in bed, diluent drinks, digitalis, and alkalies. This case, which was most closely observed, seems to point to a distinct causal connection between the uric acid and oxalates on the one hand, and the albuminuria on the other. Professor Grainger Stewart[2] refers, on the subject of "after breakfast albuminurias," to two cases among children in which breakfast was followed by the disappearance of albumen from the urine, which was present when the patients rose in the morning. May not the albuminuria here have been due to uric acid irritation, which was present especially during the night, and which disappeared on the addition of alkalies to the blood after taking food?

In all the cases referred to in this paper the uric acid and oxalates were present on naked eye or microscopic examination. I have to express my great indebtedness to Dr. Leslie Ogilvie for permission to quote several cases under his care, and to Mr. H. L. Lack, for his assistance in the examination of urines.

Case I.—A thin, neurotic boy, aged 7. Recurrent attacks of pain in back and left side, frontal headache, drowsy. Urine, specific gravity 1025. Amount normal. Blood, albumen, oxalates; casts occasionally present.

Case II.—Female, aged 11. Family history of phthisis and asthma, father suffers from gravel. A calculus in bladder had been removed by operation. Catches cold easily; neurotic. Complains of suprapubic pain. Dysuria, frequency of micturition; pain on pressure over left kidney; hæmaturia; no calculus present in bladder. Urine strongly acid; amount 10 to 15 ounces per day; blood (from kidney), albumen, pus, oxalates; bladder epithelium.

Case III.—Male, aged 11. Family history of phthisis. Had passed blood frequently in urine and gravel. Catches cold easily; well nourished, florid. Complains of severe pain right lumbar region, and tenderness there; attacks of pain during sleep; shivering; liver 2″ below costal margin. Urine acid; no albumen or blood; microscopically, numerous oxalates and a few red blood cells.

[2] *Lectures on Albuminuria.*

CASE IV.—Male, aged 6. Family history of rheumatism. Thin, neurotic. Catches cold easily, subject to skin eruptions. Complains of suprapubic pain; dysuria; no calculus present. Urine acid, offensive odour; uric acid and urates.

CASE V.—A thin, neurotic boy, aged 4. Family history of rheumatism; has had tonsillitis. Suffers from constipation; pain on defæcation; at times incontinence of fæces; micturition slow and delayed; occasional incontinence. Urine acid; uric acid and urates.

CASE VI.—A thin boy, aged 9. Family history of phthisis. Complains of diarrhœa; abdomen distended; fulness and tenderness in right iliac fossa. Urine very acid; uric acid and urates; trace of albumen.

CASE VII.—A well nourished boy, aged 8. Family history of phthisis. Suffers from recurrent attacks of abdominal pain; dysuria; pain localised in right iliac fossa, with fulness and tenderness on pressure there. Urine acid; oxalates.

CASE VIII.—See previous page.

CASE IX.—See previous page.

CASE X.—See previous page.

HEPATIC CIRRHOSIS OCCURRING IN TWO CHILDREN OF THE SAME FAMILY.[1]

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THERE is nothing in the family history of these children bearing on the disease. All were free from any signs of rickets, syphilis, or scrofula. The father and mother are temperate, and Case I never touched any alcoholic drink for eight years previous to his death, and Case II was an abstainer for four years. There was nothing peculiar regarding the diet of these children with the exception of their extreme liking for vinegar, so that they would drink it out of the bottle when sent to buy some, and would drink it when at home if their mother was out of the way.

CASE I.—Male, 11 years. Had had measles when 2 years old. In the beginning of 1887 he complained frequently of the "belly-ache" and coldness, and often had diarrhœa. In March his legs and abdomen began to swell, and he was tapped by Mr. Shorland seven times between April and the following September, when he died. During his illness he had several attacks of hæmatemesis and epistaxis, and during the last fourteen days he was frequently delirious, and had occasional twitching of his hands and attacks of abdominal pain. There was never any jaundice, and no albumen was found in the urine; his temperature was not recorded. No *post-mortem* was obtained, but I think, if taken in conjunction with the next case, there can be no doubt as to the cause of the symptoms.

CASE II.—Sister of the above, aged 10 years, had measles in 1888 and influenza in 1890. The early symptoms were the same as Case I, and began in October, 1890. During the next month she had attacks of abdominal pain, was jaundiced for three days, and the legs and abdomen commenced to swell. She was admitted into the Warminster Cottage Hospital on November 22nd, 1890, with well-marked ascites, and œdema of the legs and sacral region. The epigastric region was especially prominent and rather tender; the liver dulness extended from the third rib downwards to the costal arch, but its edge could not be felt, and there was no enlargement of the spleen. The heart was displaced upwards and outwards, but there were no signs of valvular incompetence. The skin was dry and scaly, but no nævoid marks were found; the motions were very offensive, and a little paler than normal; the urine, of which she passed 16 ounces in the first twelve hours, was high coloured, with a little albumen, but no bile or sugar, and the sediment contained some renal epithelium and blood corpuscles; temperature 98.6° morning and evening, pulse 98. There had been no hæmorrhages, and the fundus of each eye was normal. She was kept in bed and put on a milk diet, and given a pill of rhubarb and grey powder at night, followed by a scammony and jalapine draught in the morning, and during the day she took a mixture of digitalis and acetate of potash for the first fourteen days, and then quinine and iron, and by December 15th the ascites and œdema had quite gone, and she seemed practically well by January 17th, 1891, when she was discharged. She was then passing 40 to 50 ounces of urine a day with a specific gravity of 1020, containing a little albumen and a few blood corpuscles. The liver dulness measured 2 inches vertically in the nipple line. During her stay in the hospital her evening temperature was generally between 99° and 100°, and on December 22nd she had great muscular tenderness in the arms and legs, and her temperature was 100.6 and pulse 104 for two evenings. She had only been home a few days when the dropsy began to return, and she had attacks of abdominal pain and sickness, so she was readmitted on January 26th, 1891, when the dropsy was found to be more marked than when first admitted, and she was passing 8 ounces of urine in the day, containing a trace of albumen and 8.68 grammes of urea. For the next two days she was delirious at times, laughing and crying by turns; the temperature varied from 98.4 A.M. to 100.8 P.M., and she passed her motions and urine unconsciously. On January 29th she rather suddenly became comatose, with dilated pupils and rigidity of limbs, and died in a few hours without any convulsions.

On *post-mortem* examination three hours after death the abdomen contained 10 pints of fluid; there was no peritonitis or ulceration of the intestines, but the mesenteric glands were a little enlarged but not caseous. The liver was adherent to the diaphragm, yellowish-red in colour, covered with granules varying from the size of a pin's head to half a pea, very tough on section, not bile-stained, and weighed 20 ounces; the spleen weighed 2¾ ounces, and was normal in appearance and consistence; the pancreas was very hard and tough; the thoracic organs were normal; the brain weighed 32 ounces, and appeared normal to the naked eye; but, unfortunately, not having read Dr. Ormerod's[2] paper at that time, no microscopical examination was made. Sections of the liver, kidneys, and pancreas were made after hardening, and both the latter were found to be normal, but the liver showed well-marked multilobular cirrhosis, the fibrous tissue showed a great excess of small bile ducts, and staining by osmic acid demonstrated excess of fat in the cells of the periphery of the lobule. Dr. Duffin, Professor of Pathology in King's College, kindly examined my sections, and confirmed what I have already stated, and added that he was struck with the size of the remaining lobules and the good condition of their cells, so that there must have been plenty of good bile-secreting power at the time of death.

The chief points in the history of these cases are that measles was the only illness common to both, and that both very largely indulged in vinegar. Dr. Lauder Brunton has pointed out that vinegar taken for some time can lead to fatal emaciation; and I suppose by lessening the gastric secretion it so interferes with digestion as to cause the formation of digestive irritants (albumoses and allied bodies), which, after absorption by the portal system, are capable of setting up a hyperplasia of the connective tissue in connection with hepatic portal system. The symptoms which are noteworthy in these cases are the gradual onset of the disease in an indefinite manner; the various hæmorrhages, the absence of jaundice due to the stress of the disease falling on the portal system; the various nervous phenomena, namely, muscular twitchings in the boy, and delirium and coma towards the close of both cases; slight pyrexia in the evening.

On analysis of 112 cases under 18 years of age, it is seen that the part taken by alcohol and syphilis respectively as a cause of biliary cirrhosis is a much smaller one than was at one time supposed. Alcohol can be excluded in 46.4 per cent., and of the remainder it accounts for 18.7 per cent. Syphilis might be a possible cause in 16.3 per cent.; so that both taken together only account for 35 per cent., leaving nearly two-thirds of the cases attributable to other causes. Besides alcohol, other toxic substances after absorption by the hepatic circulation have been assigned as causes, namely, the malaria miasm found as a cause on the West Coast of Africa, the products of faulty digestion, and the use of too stimulating articles of diet. Dr. Eustace Smith[3] mentions two cases recorded by Wettergreen and S. West, in which drinking largely of coffee might have been the cause. Dr. Gibbons[4] has called the attention of the profession to the chief features of the disease (both inter- and intra-lobular) as seen in Calcutta, where it is practically limited to children of well-to-do Hindus, and as many as three or four children die in the same family before they reach the age of 2½ years, whilst the Mohammedan children nearly always escape. The reason of this fatality amongst the Hindus is obscure, and Dr. Alex. Crombie suggests that its prevalence being concomitant with the extension of the underground drainage system and the direct connection of this with the better class of houses, especially of the well-to-do Hindus, might offer the most likely clue to the etiology of this most remarkable disease.

The other conditions under which hepatic cirrhosis in the young occur are: (1) Congenital obstruction or deficiency of the bile duct, which by blocking back the bile causes a primary ectasis of the smaller canals, followed by extravasation of bile among the hepatic cells, and consequently their necrosis, with secondary formation of connective tissue. Drs. W. Legg[5] and H. Gibbs[6] have recorded cases which lived 5½ months and 7 months respectively. (2) Chronic venous congestion of the liver due to pulmonary or heart disease, although a frequent cause amongst adults, is very rare in childhood. (3) Pyle-phlebitis of syphilitic origin. (4) As part of a general overgrowth of fibrous tissue in several different organs due to a "fibroid diathesis." Dr. Pye-Smith[7] and Dr. Cayley[8] have recorded cases, and Dr. Burdon Sanderson suggests that the finding of pericarditis, pleurisy, and cirrhosis together points to their being the expression of some general disease of the lymphatic tissue throughout the body, inasmuch as the pleuræ and serous membranes generally, with the sheath of the biliary canals, are part of the same lymphatic system. (5) Combined with various forms of tuberculous disease. The liver may be either infiltrated with tuberculous

[1] For some of the notes of Case I I am indebted to Mr. Shorland, of Westbury; Case II I saw when under Mr. Willcox's care, and to him I am indebted for permission to publish my notes.

[2] *St. Barth. Hosp. Rep.*, vol. xxvi.
[3] *Diseases of Children*, p. 273.
[4] *Medical Annual*, 1891.
[5] *Trans. Path. Soc.*, vol. 27, p. 178.
[6] *Ibid.*, vol. 34, p. 129.
[7] *Ibid.*, vol. 33, p. 172.
[8] *Ibid.*, vol. 27, p. 194.